

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



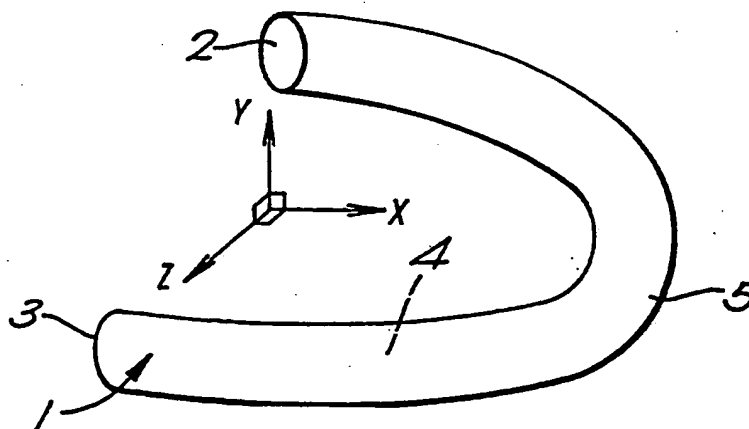
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: <b>A61F 2/06</b>	<b>A1</b>	(11) International Publication Number: <b>WO 95/09585</b>
		(43) International Publication Date: <b>13 April 1995 (13.04.95)</b>
<p>(21) International Application Number: <b>PCT/GB94/02023</b></p> <p>(22) International Filing Date: <b>16 September 1994 (16.09.94)</b></p> <p>(30) Priority Data:              9320288.5      1 October 1993 (01.10.93)      GB              9412882.4      27 June 1994 (27.06.94)      GB</p> <p>(71) Applicant (for all designated States except US): <b>IMPERIAL COLLEGE OF SCIENCE, TECHNOLOGY &amp; MEDICINE [GB/GB]; Exhibition Road, London SW7 2AZ (GB).</b></p> <p>(72) Inventor; and          (75) Inventor/Applicant (for US only): <b>CARO, Colin [GB/GB]; Imperial College of Science, Technology &amp; Medicine, Exhibition Road, London SW7 2AZ (GB).</b></p> <p>(74) Agent: <b>MARCH, Gary, Clifford; Batchellor, Kirk &amp; Co., 2 Pear Tree Court, Farringdon Road, London EC1R 0DS (GB).</b></p>		<p>(81) Designated States: <b>AU, CA, GB, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</b></p> <p><b>Published</b>  <i>With international search report.</i></p>

(54) Title: **VASCULAR PROSTHESES**

(57) Abstract

A vascular prosthesis comprising a length of generally hollow tubing having openings at both ends thereof and including at least one curved portion whose curvature extends within three dimensions of two mutually perpendicular planes such as to induce swirl flow in a liquid medium when such medium flows through said curved portion.



BEST AVAILABLE COPY

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LV	Latvia	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LT	Lithuania	TJ	Tajikistan
DE	Germany	MC	Monaco	TT	Trinidad and Tobago
DK	Denmark	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali	UZ	Uzbekistan
FR	France	MN	Mongolia	VN	Viet Nam
GA	Gabon				

- 1 -

VASCULAR PROSTHESES

The arterial system consists largely of curved and branching vessels. Arterial flow is generally laminar but is strongly influenced by inertial forces (Reynolds numbers  $\gg 1$ ). Almost all studies of arterial fluid dynamics consider the curvature and branching to be planar. The mechanics of steady flow (Reynolds number  $\gg 1$ ) in planar bends and branches are reasonably well understood and involve:

secondary motion in the plane of the bend or bifurcation; low wall shear at the inner wall of the bend (where flow separation may occur) and high wall shear at the outer wall; and low wall shear at the outer wall of a branch (where flow separation may occur) together with high wall shear at the inner wall (flow divider).

Several findings indicate that the local blood velocity field influences: (a) the dimensions and mechanical properties of vessels and the morphology, mechanics and metabolism of the endothelium (Yoshida et al, 1988), and (b) the development of vascular disease, in particular atherosclerosis (which causes heart attack and stroke) which develops preferentially in low shear regions in arteries (Yoshida et al, 1988); intimal hyperplasia (which causes the occlusion of vascular grafts) and which develops preferentially in low shear regions in side-to-side veno-arterial bypass grafts (Dobrin et al, 1988; Rittgers and Bhamhani, 1993), and thrombosis which occurs preferentially in low shear regions.

There has been limited consideration in the physiological literature of the mechanics of flow in non-planar bends and branches.

The aortic arch is recognised to curve three-dimensionally and rotational flow has been detected in the aortic arch and descending thoracic aorta (Caro et al, 1971;

- 2 -

Frazin et al, 1990).

The branching of the left common coronary artery is recognised to be non-planar and studies in a curved bifurcation model show skewing of the velocity profile away from the 'plane' of bifurcation, both upstream of the bifurcation and in a daughter tube (Batten and Nerem, 1982).

Studies of the velocity field in a realistic model of the abdominal aorta and aortic bifurcation show centrifugal effects caused by the curvature of the abdominal aorta and aortic bifurcation inducing helical flow structures and influencing the localisation of separation zones (Pedersen et al, 1992).

There has been study of the exact anatomical locations of atherosclerotic lesions and of the detailed flow patterns at these locations in transparent isolated human arteries (Asakura and Karino, 1990).

Recent model experiments by the present inventor led to an investigation as to whether non-planar curvature and branching may be more common than planar curvature and branching in the arterial tree.

With non-planar curvature and branching there is the expectation of skewing of the secondary motion (with the possible development of swirl flow) and alteration of the distribution of wall shear stress from that present with planar curvature and branching. The present inventor has undertaken several studies as a means of determining whether non-planar curvature and branching are common in the circulation. Inspection of a cast of a human aorta and of a rabbit aorta showed the origins of several branches of the aortic arch and abdominal aorta to be tangential to the axis of the parent vessel in more than one plane; non-planar curvature at some bifurcations, for example at the aortic bifurcation; and curvature of the inlet to some bifurcations in a plane other than the 'plane' of bifurcation, as at the lower abdominal aorta.

- 3 -

Phase-shift-based MRI studies have been undertaken with steady laminar flow in a planar model of the aortic bifurcation. When the inlet tube was straight, thin-slice dynamic flow imaging, sensitive to the axial component of the flow, shows the secondary motion in a daughter tube to be in the plane of bifurcation (see Figures 1 and 1A). When the inlet tube was curved in a plane normal to the plane of bifurcation, the secondary motion in the daughter tube was skewed (see Figures 2 and 2A).

Phase-shift-based MRI studies have also been undertaken on the lower abdominal aorta and aortic bifurcation in healthy human subjects. Cardiac gated projective phase contrast angiograms show the lower abdominal aorta and aortic bifurcation to be curved in a plane normal to the 'plane' of aortic bifurcation (concavity anterior) (Figs 3,4). Thin-slice dynamic flow imaging, sensitive to the axial component of the flow, shows skewing of the secondary motion in the common iliac arteries.

Other studies lead to the expectation that the velocity field at the carotid bifurcation is non-planar. Earlier MR studies in healthy human subjects showed the common carotid arteries to be curved in the antero-posterior plane (Caro et al, 1992). Anatomical studies show that the common carotid artery bifurcation does not lie in the antero-posterior plane.

Non-planar curvature and branching have been found to be relatively common in the arterial tree. Non-planar curvature and branching have been found to influence the blood velocity field and may therefore influence vessel biology and the development of vascular disease. From a limited knowledge of vascular bypass surgery, it appears that side-to-side anastomosis, as conventionally performed, involves the construction of a planar bifurcation/confluence (Dobrin et al, 1988; Eastcott, 1992). Side-to-Side anastomoses are prone to fail from intimal hyperplasia,

- 4 -

which is associated with low local blood velocity and possibly low local wall shear stress (Dobrin et al, 1988).

In the light of these various findings the present invention has been developed.

According to this invention there is provided a vascular prosthesis comprising a length of generally hollow tubing having openings at both ends thereof and including at least one curved portion whose curvature extends within three dimensions of two mutually perpendicular planes such as to induce swirl flow in a liquid medium when such medium flows through said curved portion.

In another aspect we provide a vascular prosthesis comprising at least one hollow body portion from which at least one branch member extends at an intersection between the body portion and said branch member, characterised in that said at least one branch member is of a shape and/or orientation with respect to the body portion such that at least part of said member extends in a non-planar configuration.

At least a section of the said at least one branch member may extend in a plane which is different from that plane of the body portion which includes the central axis of the body portion and the centre of said intersection between body portion and branch member.

Preferably a major part of the branch member may be curved so as to extend at an acute angle with respect to the body portion.

Preferred features of the invention are to be found in the sub claims.

In order that the invention may be illustrated and readily carried into effect, embodiments thereof will now be described by way of example only with reference to the accompanying drawings and wherein:

Figure 1 shows a phase-shifted magnetic resonance image (MRI) of a planar model of aortic bifurcation with

- 5 -

straight inlet, mapping the axial velocities in the daughter tube,

Figure 1A shows the physical form of the planar model of the aortic bifurcation which produced the image map shown in Figure 1,

Figure 2 shows a similar image map as in Figure 1, but wherein the inlet tube was curved perpendicularly to the plane of bifurcation, mapping axial velocities also in the daughter tube,

Figure 2A shows the physical form, including curvilinear variations thereof, of the non-planar model of the aortic bifurcation which produced the image map shown in Figure 2, and including primary tube 1 or curved tube 1c, daughter tubes 1A and 1B or when curved 1D,

Figure 3 shows a cardiac gated projective phase contrast thoracic aorta angiogram, right-left coronal view,

Figure 4 shows the posterior-anterior sagittal view of the angiogram shown in Figure 3,

Figure 5 shows one embodiment of a prosthesis including a part helical section,

Figure 6 shows a further embodiment of a suitable prosthetic arterial or venous bypass, and

Figure 7 and 8 shows an alternative arrangement of prosthetic implant.

Referring to the drawings, the views of Figures 1 to 4 inclusive have already been identified and explained in the introduction hereto.

Figure 5 shows an embodiment of a prosthesis which comprises a length of generally hollow tubing 1 with openings 2,3 at each end which are adapted for surgical connection to a vein or artery by the provision of suitably shaped flanges. Blood from the circulatory system can flow from inlet 2 to outlet 3 along the hollow interior 4. The curved portion 5 is part helical in that the curvature extends within the X-Z horizontal plane and the mutually

- 6 -

perpendicular X-Y plane. Such non planar curvature induces a swirl to the flow to improve circulation and resist the formation of potentially damaging blockages within the interior. The tubing can be made of suitable bio-compatible material and such materials are commercially available and known to those skilled in the art. In order to maintain the tubing open and prevent collapse or kinking it is possible to use a stent or other structural support of plastic, metal or other material internally, externally or integral to the wall of the tubing.

In the Figure 6 arrangement, showing an arterial (or venous) bypass prosthesis in place, an artery 6 with internal blockage 7 is bypassed by means of a prosthesis according to the invention. The tubing 1 can be of similar shape, size and conformation as that shown in Figure 1, or the helical proportion can be even shorter in length e.g. less than one half of one turn or revolution. The inlet 2a and outlet 3a flanges have been surgically fastened by stitching to regions of the artery remote from the blockage. Swirl flow is induced by skewing of the blood flow within the non-planar curved portion 5, to improve flow characteristics and reduce the potential for deposit build up.

Figures 7 and 8 show different arrangements wherein a non planar curved branch member 8 extends from an opening in a hollow body portion 9, which latter may be inserted within a vein or artery either for receiving flow of blood from the said branch member, or for delivering a flow of blood thereto, wherein a swirl flow is established within the non-planar curved branch member.

Figure 9 shows one form of surgical connection between a prosthesis 1 having spirally curved portion 5 and a blood carrying vessel 7. The connection between the prosthetic tube 1 and vessel 7 is in the nature of an offset 'plumber's' joint, improving flow to or from the vessel,



- 7 -

wherein swirl flow is induced within the prosthesis.

Moreover, prosthetic devices according to the invention can include branching such as bifurcation. Indeed an example of a prosthesis is shown in Figure 2A, particularly including the curved portions 1C and/or 1D.

#### References

Asakura, T., and Karino, T. (1990). Flow patterns and spatial distribution of atherosclerotic lesions in human coronary arteries. *Circulation Research* 66, 1045-1066.

Batten, J. R. and Nerem, R. M. (1982). Model study of flow in curved and planar arterial bifurcations. *Cardiovasc. Res.* 16, 178-186.

Caro, C. G., Fitz-Gerald, J. M. and Schroter, R. C. (1971). Atheroma and arterial wall shear. *Proceedings of the Royal Society, London, Series B*, 177, 109-159.

Caro, C. G., Dumoulin, C. L., Graham, J. M. R. and Souza, S. P. (1992). Secondary flow in the human common carotid artery imaged by MR angiography. *J. Biomech. Eng.* 114, 147-149.

Dobrin, P. B., Litooy, F. N., Golan, J., Blakeman, B. and Fareed, J. (1988). Mechanical and histologic changes in canine vein grafts. *J. Surg. Res.* 44, 259-265.

Eastcott, H. H. G. (1992). *Arterial Surgery*, 3rd Edition, Churchill-Livingstone, Edinburgh.

Frazin, L. J., Lanza, G., Vonesh, M., Khasho, F., Spitzzeri, C., McGee, S., Mehlman, FD., Chandran, K. B., Talano, J. and McPherson, D. (1990). Functional chiral asymmetry in descending thoracic aorta. *Circulation* 82, 1985-1994.

Rittgers, S. E. and Bhambhani, G. H. (1993). Doppler color flow images of iliofemoral graft end-to-side distal anastomotic models. *Ultrasound Med. Biol.* 19, 257-267.

Yoshida, Y., Yamaguchi, T., Caro, C. G., Glagov, S. and Nerem, R. M. (1988). Eds: *Role of Blood Flow in Atherogenesis*. Tokyo: Springer-Verlag.

- 8 -

CLAIMS

1. A vascular prosthesis comprising a length of generally hollow tubing having openings at both ends thereof and including at least one curved portion whose curvature extends within three dimensions of two mutually perpendicular planes such as to induce swirl flow in a liquid medium when such medium flows through said curved portion.
2. A prosthesis as claimed in claim 1 wherein the ends of the tubing are adapted to permit surgical connection to the vascular system.
3. A prosthesis as claimed in claim 1 or 2 wherein the curved portion is part helical in that the length of its curve is less than one complete turn.
4. A prosthesis as claimed in any preceding claim which is constructed from a resiliently flexible bio-compatible material.
5. A vascular prosthesis comprising at least one hollow body portion from which at least one branch member extends at an intersection between the portion and said branch member, characterised in that said at least one branch member is of a shape and/or orientation with respect to the body portion such that at least part of said member extends in a non-planar configuration.
6. A vascular prosthesis as claimed in claim 5 wherein a section of the said at least one branch member extends in a plane which is different from that plane of the body portion which includes the central axis of the body portion and the centre of said intersection between body portion and branch

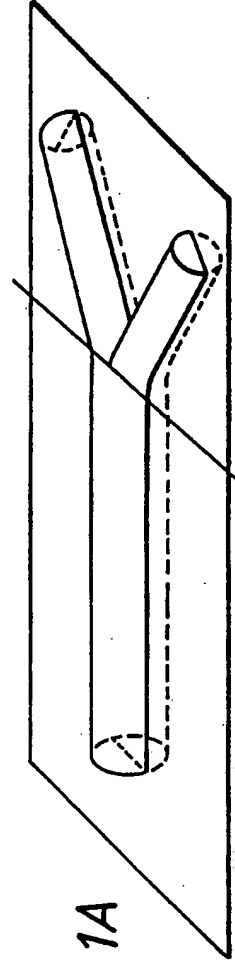
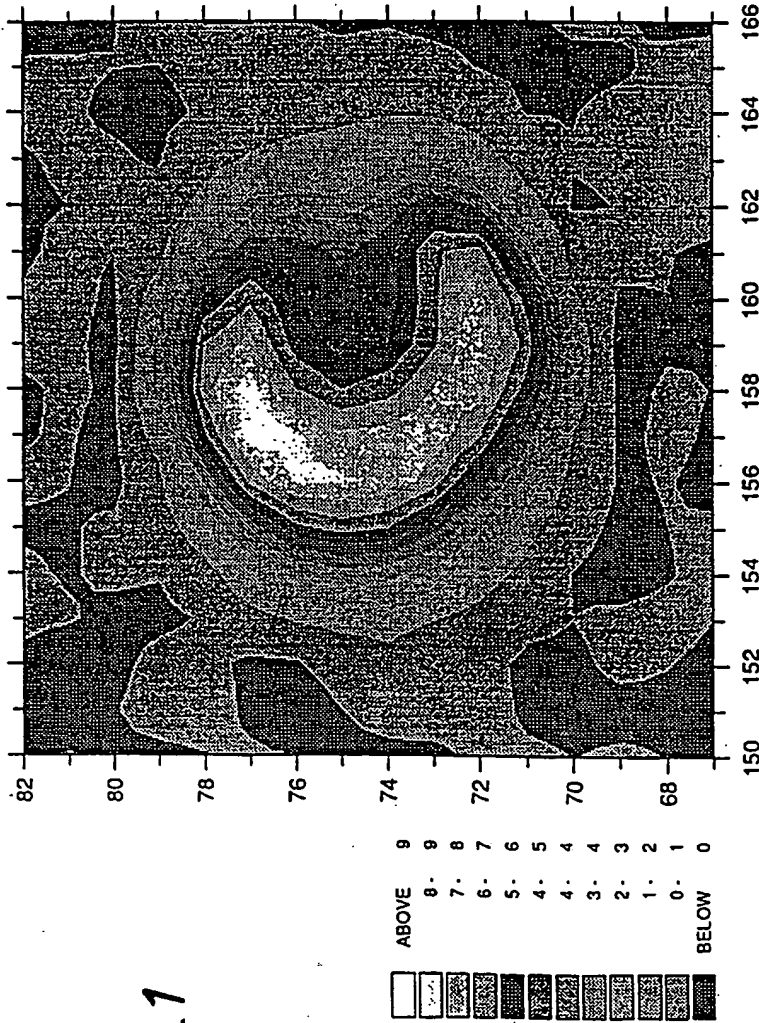
- 9 -

member.

7. A vascular prosthesis as claimed in claim 5 or 6 wherein a major part of the branch member may be curved so as to extend at an acute angle with respect to the body portion.

8. A vascular prosthesis as claimed in any preceding claim in combination with a vascular joining segment of generally tubular form having a hollow protuberance locatable within an end of said tubing or branch member.

1/5



2/5

FIG. 2

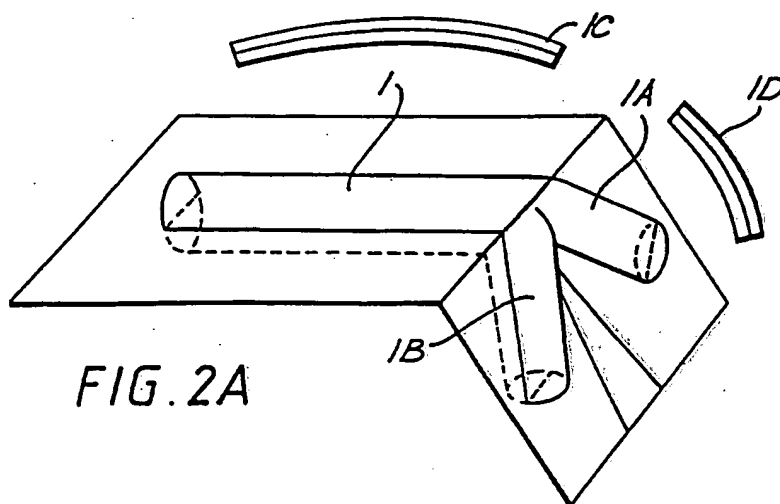
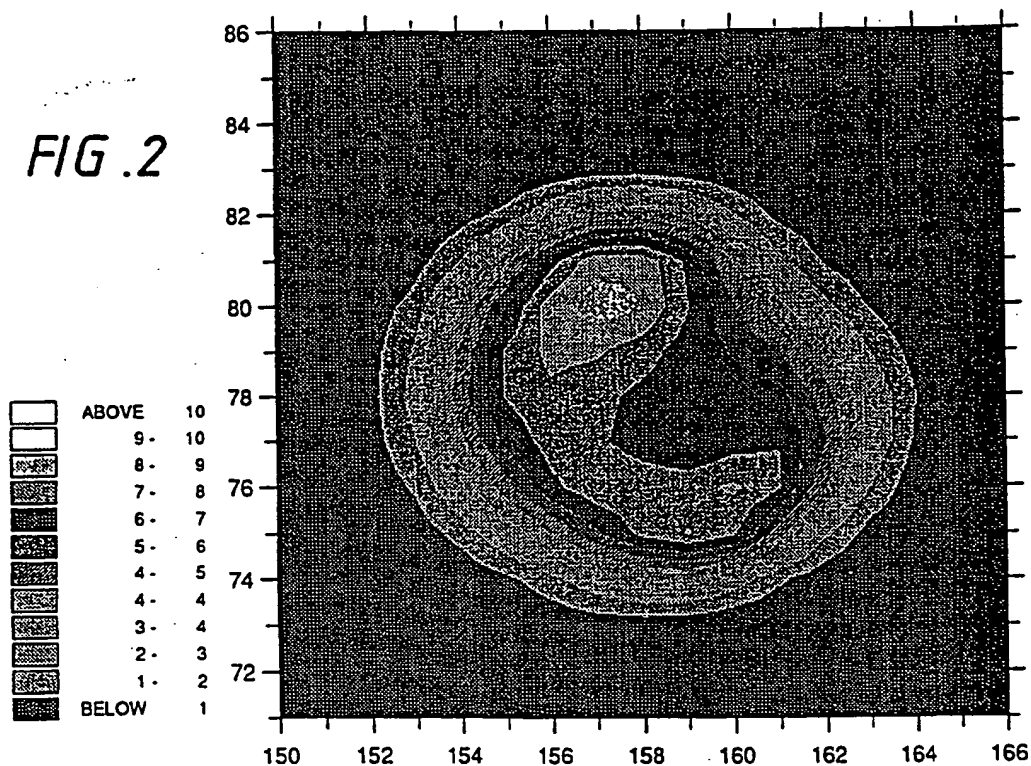


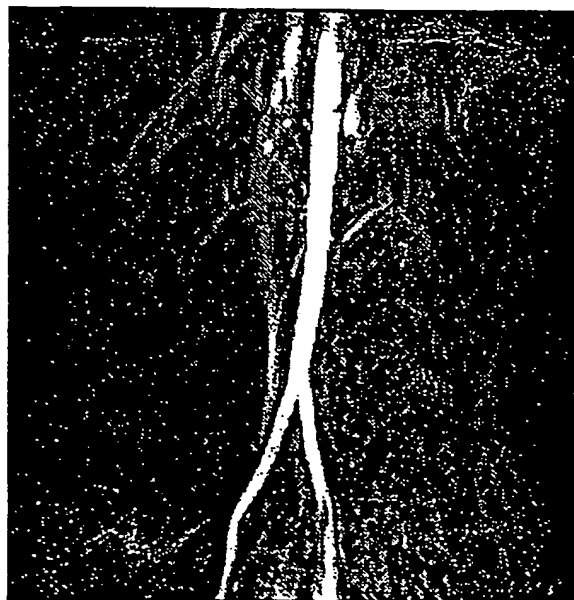
FIG. 2A

3/5

THORACIC AORTA

FIG. 3

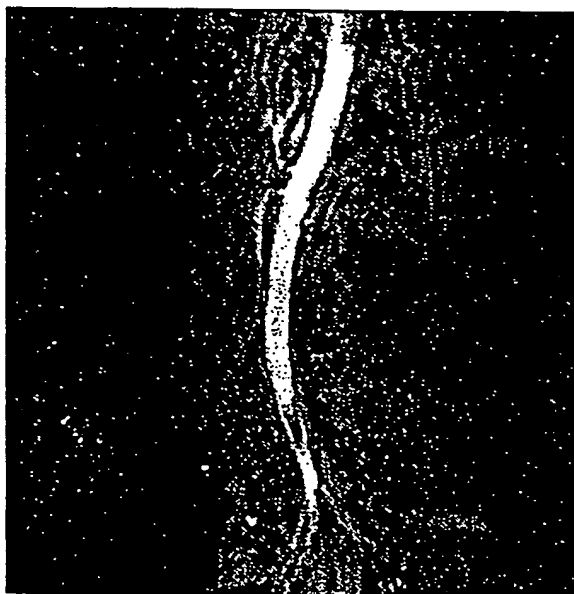
RIGHT



LEFT  
CORONAL VIEW

FIG. 4

POSTERIOR



ANTERIOR  
SAGGITAL VIEW

4/5

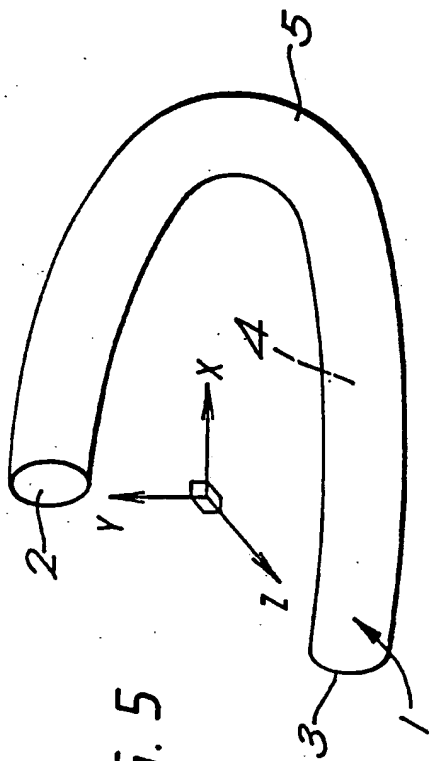


FIG. 5

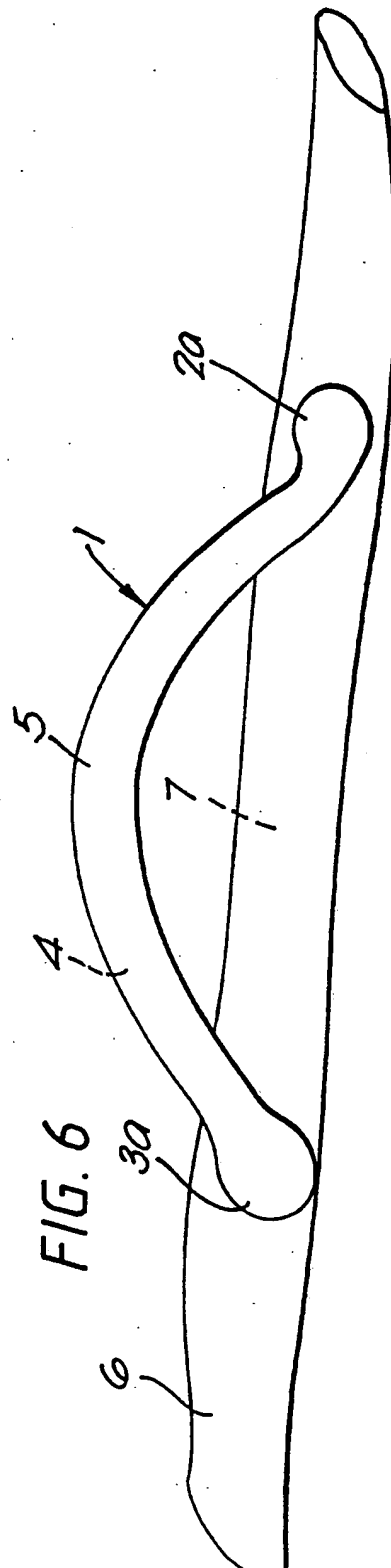


FIG. 6

5/5

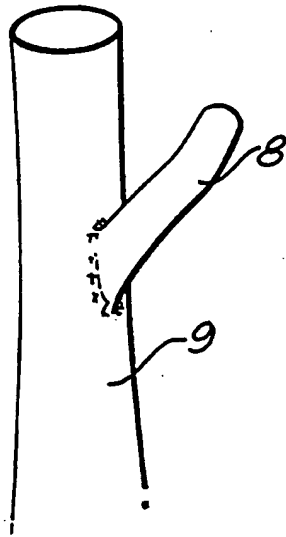


FIG. 7

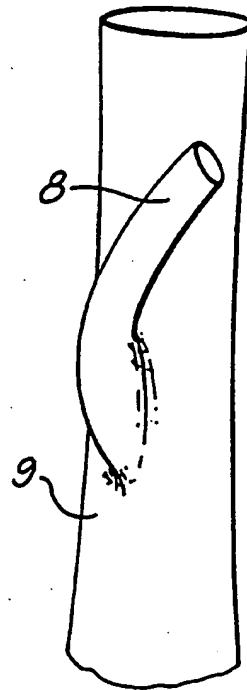


FIG. 8

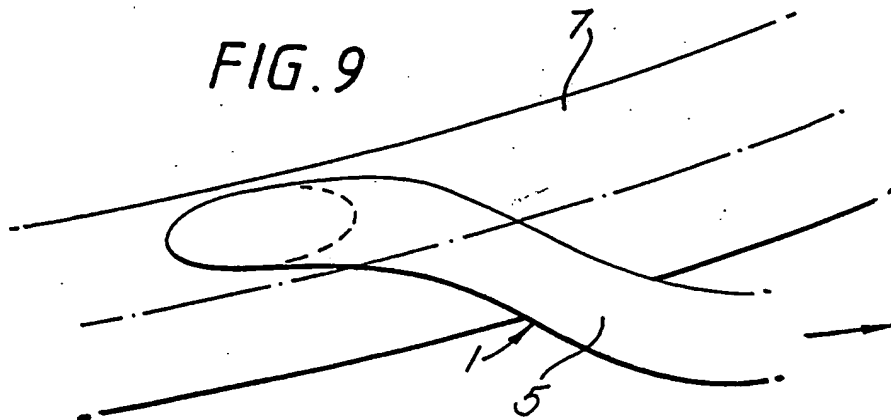


FIG. 9



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 94/02023

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61F2/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CIRCULATION, vol.82, no.6, December 1990, DALLAS TX, USA pages 1985 - 1994 L.J. FRAZIN ET AL. 'FUNCTIONAL CHIRAL ASYMMETRY IN DESCENDING THORACIC AORTA' cited in the application	1-4
Y	see page 1993, column 1, line 45 - column 2, line 2 cited in the application	5-8
Y	FR,A,2 666 502 (D. ROUX) 13 March 1992 see abstract; figure 1 see page 3, line 37	5-7
Y	US,A,5 156 619 (W.K. EHRENFELD) 20 October 1992 see abstract; figures	8
	--- -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*A\* document member of the same patent family

Date of the actual completion of the international search

24 November 1994

Date of mailing of the international search report

19.12.94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Wolf, C

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 94/02023

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,4 938 740 (J. MELBIN) 3 July 1990 see column 5, line 10 - line 25; figure 4 ----	1
A	EP,A,0 503 101 (V.V. KESHELAVA) 16 September 1992 see column 4, line 41 - column 5, line 16; figures ----	1,2
A	US,A,4 313 231 (K. KOYAMADA) 2 February 1982 see the whole document ----	1,2,4,8
A	WO,A,93 02637 (NEWTEC VASCULAR PRODUCTS) 18 February 1993 ----	
A	US,A,5 139 515 (F.ROBICSEK) 18 August 1992 -----	

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International Application No  
**PCT/GB 94/02023**

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
FR-A-2666502	13-03-92	NONE		
US-A-5156619	20-10-92	NONE		
US-A-4938740	03-07-90	US-A-	5104402	14-04-92
EP-A-0503101	16-09-92	JP-T-	4506765	26-11-92
		WO-A-	9114407	03-10-91
US-A-4313231	02-02-82	NONE		
WO-A-9302637	18-02-93	AU-A-	2329892	02-03-93
		EP-A-	0596905	18-05-94
US-A-5139515	18-08-92	NONE		

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☒ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**